

REMARKS

I. Claims in the Case

Claims 5, 10, 21 and 25 has been amended. Claims 5, 7-10, and 13-29 are pending, of which claims 8, 9, 15, 17-20 and 22 are withdrawn. Claims 5, 7, 10, 13, 14, 16, 21 and 23-29 are currently under examination.

II. Rejections Under 35 U.S.C. §112, Second Paragraph

To address the Action's concerns with respect to claims 10, 21 and 25 under 35 U.S.C. §112, second paragraph, these claims have been amended to insert the ATCC deposit number of a hybridoma producing antibodies recognizing the identified antigen. Also enclosed is a copy of a declaration and ATCC receipt submitted in parent application 08/251,574 (now US patent 6,750,329). The specification has also been amended in the same manner found acceptable in respect of the '329 patent.

III. Rejections Under 35 U.S.C. §112, First Paragraph

With respect to the written description rejections of claim 10, 21 and 25 under 35 U.S.C. §112, first paragraph, it is submitted that the comments in the foregoing section are equally applicable to obviate this rejection, particularly in light of the fact that such was found acceptable with respect to the recently issued parent '329 patent.

IV. Anticipation Rejections -- Rejections of claims 5, 7, 21, 24, 25, 28 and 29 over US 4,590,071

The Action first rejects claims 5, 7, 21, 24, 25, 28 and 29 as anticipated by US patent 4,590,071 (the '071 patent), as evidenced by Kirkwood *et al.* Applicants respectfully traverse.

First, claim 5 has been amended in a manner that is not believed to in any way alter its scope, but to clarify that the claim includes the step of "determining that the cells of the patient's cancer express a selected cell surface associated antigen." This step was previously in claim 5 in

a slightly different form, stated as “wherein it has been determined that cells of the patient’s cancer express an antigen recognized and bound by the protein.” Regardless, in the case of the present or previous language of claim 5, for the reasons set forth below it is submitted that the Action fails to set forth a *prima facie* case of anticipation.

The improvement embraced by the invention of claim 5 is the realization that it is important to treat only those patients that have tumors expressing the particular antigen that is targeted by the immune conjugate. Thus, the claims are directed to the concept of first determining that the particular patient’s cancer actually expresses a selected cell-surface associated antigen, wherein the antigen is capable of being recognized and bound by a protein bearing an antigen recognition site.

In this regard, we have carefully reviewed the ‘071 patent and can find no teaching relevant to the step of first determining whether the cells of the patients’ cancer express an appropriate target antigen. Perhaps we have overlooked a relevant passage, in which case the Examiner is requested to identify such a teaching. This step is important in that it avoids the situation of needlessly treating patients whose cancer do not express the appropriate antigen. This is explained in the current specification at the top of page 15:

Administration of the immunoconjugates of the present invention to an individual who has been diagnosed as having a tumor with a specific antigenic determinant will allow targeting and concentration of the cytotoxic agent at the site where it is needed to kill the tumor cells. *By so targeting the cytotoxic agents, non-specific toxicity to other organs, tissues and cells will be eliminated or decreased.*

(emphasis supplied). In contrast, the ‘071 patent teaches an entirely opposite approach to ensuring that a particular tumor will be targeted – rather than teaching to select patients on the basis of the antigen begin targeted, it teaches instead to prepare a “cocktail” that has a mixture of different targeting moieties. See, e.g., ‘071 patent at col. 5, lns 45-50. The reason for this

teaching is evident from a further reading of the '071 spec, which teaches that not all melanomas are recognized by the "XMMME-001-RTA" conjugate (col. 6, lns 22-23). However, instead of teaching one to simply pre-test the tumor and treat only the appropriate ones, it teaches to make a mixture of immunoconjugates – thus teaching away from the present invention.

For the foregoing reasons, the Action has failed to make out a *prima facie* case of anticipation with respect to any of claims 5, 7, 21, 24, 25, 28 or 29.

V. Obviousness Rejections

A. Rejection of claims 5, 26-29

The Action next rejects claims 5 and 26-29 as obvious over the combination of the '071 patent in view of US 4,753,894 (the '894 patent). Applicants again respectfully traverse.

Applicants observations with respect to the '071 patent are set forth above and are incorporated here.

The '894 patent is said by the Action to teach "methods of diagnosing and treating cancer in patients by administering monoclonal antibodies that selectively bind said cancer," and refers to col. 3, lns 45-48; col. 4, lns 1-5 and lns 38-41. Applicants totally disagree. The '894 patent simply refers to selecting antibodies on the basis of their "selectivity for human breast cancer cells and the range of human breast cancer cells to which they bind." Col. 3, lns 19-21. The patent goes on, at col. 3, lns 24-45, that this can be achieved by screening against "panels" of human breast cancer cell lines. This is in no way commensurate or even relevant to the present invention, which is directed to testing the actual tumor cells of the actual patient that is to be treated. Furthermore, we have reviewed the excerpts referred to by the Action and find no teaching or suggestion of testing the actual patient that is to be treated. If the Examiner is aware

of any such teaching in the '894 patent, she is respectfully requested to specifically identify such passage.

For the foregoing reasons, no *prima facie* obviousness rejection has been made with respect to claims 5 and 26-29 over the '071 patent in view of the '894 patent.

B. Rejection of claims 5, 13, 14 and 16

The Action next rejects claims 5, 13, 14 and 16 as obvious over the combination of the '071 patent in view of Blick *et al.* ("Blick"). Applicants again respectfully traverse.

Applicants comments above with respect to the '071 patent are incorporated herein.

Blick is cited for the proposition that Blick teaches treating cancer with TNF-alpha and thus obviates the use of TNF-alpha as a biological response modifier in the context of the current claims.

In response, the Action fails to in any way attempt to show how these teachings are combinable, and thus fails to set forth a *prima facie* case of obviousness. The '071 patent refers specifically and only to the use of toxic "lectins" as the toxic portion of the immunoconjugate. See, *e.g.*, the "Summary of the Invention" beginning at col. 1, line 55. There is no teaching or suggestion anywhere that we can find to use any other type of toxic substance. The Action fails to indicate how one of skill would have understood that a teaching to use a "lectin" would be in any way equated with a cytokine like TNF.

Similarly, there is no teaching that we can find anywhere in Blick that would suggest to one of skill to *target* TNF to tumor cells using an immunoconjugate. On the contrary, to the extent that Blick indicates that rTNF is active all by itself we can find no basis for any teaching to use a targeted approach, and certainly no basis to conclude that a targeted approach would be active, or that a TNF immunoconjugate would maintain its TNF activity.

For the foregoing reasons, it is evident that no *prima facie* case of obviousness has been set forth in that there is no basis for concluding that the references are properly combinable.

C. Rejection of claims 5 and 23

Lastly, the Action rejects claims 5 and 23 as obvious over the combination of the '071 patent in view of Ghose *et al.* ("Ghose").

Applicants first incorporate by reference its comments with respect to the '071 patent.

The Ghose reference is cited for the proposition that it teaches the advantages of using a fused immunoconjugate as opposed to a chemically conjugated immunoconjugate.

In response, Applicants have reviewed the excerpt in Ghose referred to by the Action at page 334, presumably:

Genetic engineering is also likely to provide in the not far distant future tailored antibody molecules with appropriate polypeptide chains for optimal conjugation to a given protein toxin or chemotherapeutic agent. This will include hybrid antibody molecules (already constructed by chemical methods) that have one arm of the IgG directed against the TAA and the other against the protein toxin.

Page 334, lines 13-18. However, this excerpt simply states that genetic engineering is "likely" to provide such constructs in the "not far distant" future. Such teaching is certainly insufficient to teach one of "ordinary" skill that the invention has a likelihood of being successfully enabled. How far is the "not far distant" future? Two years? Three years? We note that the priority date of the present case is less than two years after the publication of Ghose.

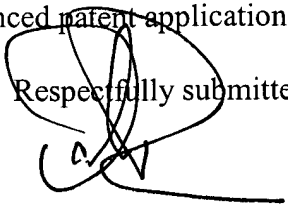
We submit that, once again, for the reasons stated above, no *prima facie* case of obviousness has been made with respect to the subject matter of claims 5 and 23.

VI. Conclusion

For the foregoing reasons, it is submitted that the present case has been shown to be in condition for allowance.

The Examiner is invited to contact the undersigned attorney with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,


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